**Health and Drug Alerts**

Paroxetine (Paxil) and congenital malformations

Reason for posting: Selective serotonin reuptake inhibitors (SSRIs) have not previously been demonstrated, as a group, to be teratogenic.1 However, the results of an unpublished study2 by GlaxoSmithKline (GSK) has led the US Food and Drug Administration and Health Canada to warn that one SSRI, paroxetine, may increase the risk of major congenital malformations.3

The drug: Antidepressants, including paroxetine, are used to treat major depression, anxiety, obsessive–compulsive disorder and premenstrual dysphoria, all common disorders during the childbearing years.4 GSK, the manufacturer of paroxetine and another antidepressant, bupropion, recently completed an unpublished retrospective study of data from 2 US managed-care insurance databases. Pregnancy outcomes among 3581 expectant mothers aged 12–49 years who were taking antidepressants were studied.

Initially, the study sought to investigate whether women prescribed bupropion had infants with higher rates of cardiovascular malformations than women either taking other antidepressants or taking the drug in the third trimester only. Any cardiac or serious congenital malformation was recorded for users of bupropion in the first or third trimester and users of any other antidepressants. The analysis excluded women with concurrent first-trimester use of known teratogens, including lithium, valproic acid and carbamazepine.

Children exposed to bupropion in the first or third trimester did not have increased rates of cardiovascular malformations than women either taking other antidepressants or taking the drug in the third trimester only. Any cardiac or serious congenital malformation was recorded for users of bupropion in the first or third trimester and users of any other antidepressants. The analysis excluded women with concurrent first-trimester use of known teratogens, including lithium, valproic acid and carbamazepine.

Only users of paroxetine had an increased risk of malformations higher than those of other antidepressants (Table 1). Various organ systems (gastrointestinal, genitourinary and central nervous system) were affected in roughly equal proportions. The most common cardiovascular malformations seen were ventricular septal defects.2

The absolute rate of major congenital seen in the first trimester for paroxetine users was 4%; of cardiovascular malformations, 2%.3 This study did not include controls of women not taking an antidepressant; however, the prevalence of major congenital and cardiovascular malformations for all births in the United States, regardless of drug exposure, are 3% and 1%, respectively.3

What to do: This study is limited by its retrospective design, its post hoc secondary analyses, the limited clinical details available in an insurance database, and its lack of controls. However, it is one of the first reasonably large epidemiologic studies to suggest possible teratogenicity of an SSRI. Why paroxetine may have this effect is not clear, and the results conflict with other epidemiologic studies performed to date.3 Although the relative risk increase of malformations is about twofold, the absolute risk increase over baseline malformation rates appears to be about 1% (i.e., about 100 pregnant users would be needed before additional harm would come to one infant). Any woman of childbearing age being treated with paroxetine should be counselled on these absolute and relative risks. If pregnancy is a real possibility, consideration should be given to switching medications.

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REFERENCES


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Books Received